White matter integrity and cognitive ageing: a combined diffusion tensor and magnetization transfer MRI study

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Introduction

The pivotal role played by the brain's white matter in successful cognitive ageing is increasingly acknowledged. Imaging has shown that white matter integrity is highly dependent on age. Therefore, understanding relationships between white matter structure and cognitive ageing is assisted when the age range of samples of elderly people is narrow, or the studies are longitudinal in design. Furthermore, information on prior mental ability, ideally measured early in life, may be key to elucidating the underlying associations between imaging biomarkers of white matter integrity and age-related changes in cognitive ability [1]. Here we present interim data from a unique cohort of subjects, termed the Lothian Birth Cohort 1936 (LBC1936) [2]. These subjects, who were born in 1936 and underwent cognitive testing in 1947 at age 11, are currently undergoing brain imaging and repeat cognitive testing in their early 70s. These data are used to test the hypothesis that white matter integrity, as measured by diffusion tensor (DT-MRI) and magnetization transfer (MT-MRI) MRI, is related to cognitive ability in youth and current age, and efficiency of the brain's information processing.

Methods

Subjects: From the 1091 members of the LBC1936, 75 were recruited for brain imaging between November 2007 and April 2008. No subject had a history of dementia, and all have Mini-Mental State Examination scores of 24 or higher.

Cognitive tests: Subjects' IQ was tested at age 11 in June 1947 using a version of the Moray House Test (MHT) of verbal reasoning. Between 2004 and 2007 they took a battery of mental tests, including the same version of the MHT they took approximately 60 years earlier, a subset of WAIS-III performance tests, and measures of information processing speed (simple and 4-choice reaction times, and inspection time).

MRI acquisition: All MRI data were obtained using a GE Signa LX 1.5 T clinical scanner. The MRI examination consisted of standard structural (T_1-, T_2- and FLAIR-weighted FSE), DT-MRI and MT-MRI. To provide isotropic whole brain coverage, all sequences imaged 72 contiguous axial slice locations with a FOV of 256 × 256, matrix 128 × 128 and slice thickness 2 mm. The MT-MRI protocol consisted of two standard SE sequences (TR/TE 3525/10 ms); one with a MT saturation pulse applied 1 kHz off resonance and one without. In the DT-MRI experiment, diffusion-weighted (DW) images were acquired using a single-shot spin-echo echo-planar (EP) imaging sequence (TR/TE 16500/95.5 ms). Sets of axial DW-EP images (b = 0 and 1000 s/mm^2) were collected with diffusion gradients applied sequentially along 64 non-collinear directions.

Image processing: After removal of bulk patient motion and eddy current induced artifacts using FLIRT, maps of mean diffusivity (<D>), fractional anisotropy (FA) and magnetization transfer ratio (MTR = $100\{M_0-M_s\}/M_0$, where M_s and M_0 are signal intensities with/without the saturation pulse) were generated for each slice in every subject on a voxel-by-voxel basis.

ROI analysis: Values of <D>, FA and MTR were obtained for normal-appearing frontal and occipital periventricular white matter, and centrum semiovale from multiple 6 × 6 mm (3 × 3 voxels) square regions-of-interest (ROI). The observer was blind to the clinical status and cognitive function of the participants.

Statistical analysis: Correlations between imaging biomarkers and cognitive test scores were performed using Pearson's *r*. All cognitive ability indicators were adjusted for age in days at the time of testing. IQ change (age 70 IQ controlling for age 11 IQ) was measured as a regression residual. A general factor of cognitive ability (*g*) was extracted as the first unrotated principal component of the 6 WAIS-III-subtests, and a g_{speed} factor was extracted as the first unrotated principal component of 4-choice reaction time mean, simple reaction time mean (log), and inspection time mean.

Results

Sixty-seven subjects (41 men) provided both imaging and cognitive data. The table shows the resulting correlations (*r*) between the imaging biomarkers and cognitive test data. Significant correlations were seen between g_{speed} and MTR in all three regions, *g* and MTR in occipital white matter, and age 11 IQ and IQ change and centrum semiovale FA.

	Frontal white matter			Occipital white matter			Central semiovale		
	<D>	FA	MTR	<D>	FA	MTR	<D>	FA	MTR
Age 11 IQ (MHT)	-0.05	0.03	-0.07	0.05	-0.02	0.08	-0.17	**0.32****	0.10
Age 70 IQ (MHT)	0.08	-0.20	-0.09	0.04	-0.06	0.16	0.05	0.07	-0.01
IQ change 11-70	0.13	-0.22	-0.01	0.09	-0.04	0.09	0.23	**-0.26***	-0.12
G	-0.02	-0.12	-0.03	-0.19	0.00	**0.30***	-0.12	0.24	0.13
g_{speed}	-0.06	-0.05	**-0.30***	0.12	-0.06	**-0.39****	0.14	-0.13	**-0.32****

Correlations significant at the $p < 0.05$ (*) and $p < 0.01$ (**) levels. MHT: Moray House Test

Conclusions

These results provide further evidence that white matter integrity, as assessed by DT-MRI and MT-MRI, is related to life-long cognitive traits and current estimates of information processing speed. They also replicate our previous novel finding of an association between age 11 IQ and centrum semiovale FA measured in an older cohort (LBC1921) [1]. Interestingly, however, they also show that MTR correlates with information processing speed, a relationship that was not seen in the older, smaller LBC1921 cohort. Brain imaging and cognitive data collection are ongoing, with the intention to recruit and re-test as many of the LBC1936 as possible.

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References

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